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## Obesity Prevention

# Systematic review of long-term lifestyle interventions to prevent weight gain and morbidity in adults

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## Summary

The aim of this article is to determine the effectiveness of long-term lifestyle interventions for the prevention of weight gain and morbidity in adults. Prevention of weight gain is important in adults who are of normal weight, overweight and obese. A systematic review of controlled trials of lifestyle interventions in adults with a body mass index of less than 35 kg $m^{-2}$ with at least 2 years of follow-up was carried out. Eleven of 39 comparisons produced significant improvement in weight between groups at 2 years or longer with mean difference weight change ranging from −0.5 to −11.5 kg. Effective interventions included a 600 kcal/day deficit diet deficit/low-fat diet (with and without meal replacements), low-calorie diet, Weight Watchers diet, low-fat non-reducing diet, diet with behaviour therapy, diet with exercise, diet with exercise and behaviour therapy. Adding meal replacements to a low-fat diet (with and without exercise and behaviour therapy) produced significant improvement in weight. Head-to-head interventions failed to show significant effect on weight with the exception of a Mediterranean diet with behaviour therapy compared with low-fat diet. Diet with exercise and/or behaviour therapy demonstrated significant reduction in hypertension and improvement in risk of metabolic syndrome and diabetes compared with no treatment control. Lifestyle interventions demonstrated significant improvement in weight, reduction in hypertension and reduction in risk of type 2 diabetes and the metabolic syndrome.

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## Introduction

Obesity and related disease present a public health crisis. Energy-dense diets and sedentary lifestyles are associated with obesity. Changing behaviours to reduce disease burden is recognized on a European and global scale through the EU Platform for Action on Diet, Physical Activity and Health (1) and the WHO global strategy on diet, physical activity and health (2). The UK government obesity strategy and £75m campaign (3) are in response to the National Institute for Health and Clinical Excellence (NICE) obesity guidance (4) and future predictions in the Foresight report (5). Through the Change4Life campaign (3), the UK Department of Health is providing £30m to help nine towns encourage healthy lifestyles (6).

These initiatives are underpinned by evidence from interventions that focus on changing behaviours. An earlier review (7) of obesity treatments recommended that a systematic review of interventions to prevent obesity should be undertaken.

This systematic review is the first phase of the National Prevention Research Initiative-funded economic evaluation of obesity prevention for UK adults. The objective is to determine the effectiveness of interventions that focus on improving diet and activity behaviours in adults who are of normal weight, overweight and obese, to prevent weight gain and morbidity in the long-term.

## Methods

Included were randomized controlled trials (RCTs) and controlled before and after studies (CBAs) of a lifestyle interventions (diet, exercise, behaviour, environmental) in adults (18–65 years) with body mass index (BMI) <35 kg $m^{-2}$ reporting weight at least 2 years post randomization. Data were also extracted for risk factors, morbidity and mortality. The amount and distribution of fat determine the risk of obesity-related diseases and in general the more overweight the greater the risk. Adults classified as pre-obese (BMI 25.0–29.9 kg $m^{-2}$) or obese class 1 (BMI 30.0–34.9 kg $m^{-2}$) are an important target group for the prevention of weight gain because they have an increased risk of elevated risk factors for disease and obesity-related morbidities, such as dyslipidaemia, hypertension, impaired glucose tolerance (IGT), metabolic and hormonal changes, which in turn contribute to cardiovascular disease, cancers, metabolic and endocrine diseases, such as type 2 diabetes, and osteoarthritis.

Diet categorization included: 600 kcal/day deficit diet deficit/low-fat diet, low-calorie diet (1000–1600 kcal/day deficit diet), very-low-calorie diet (VLCD) (<1000 kcal/day deficit diet). Interventions were categorized as interventions with definite intention to lose weight (clearly targeted calorie reduction) and interventions with no definite intention to lose weight (no target for weight loss). No type of diet was excluded. If an intervention included two or more diets, the most stringent calorie restriction was used to classify the diet.

For exercise or behaviour therapy interventions study investigators had to give a detailed description of the components of the intervention and details of the theory underpinning the behavioural intervention.

Interventions targeting smoking cessation or salt reduction in addition to weight loss were not included. Studies were excluded in participants with eating disorders, pregnant women and severely mentally or physically handicapped adults. Studies in non-white populations were included if the ethnic group and setting were relevant to the UK ethnic population.

The literature search involved four phases (see Appendix S1 for search strategies). Phase one: primary studies identified from two systematic reviews (4,7). Phase two: CAB Abstracts, CDSR, CINAHL, DARE, EMBASE, MEDLINE and PsycINFO were searched and systematic reviews were screened for primary studies. Phase three: CAB Abstracts, CCTR, CINAHL, EMBASE, MEDLINE and PsycINFO were searched for primary studies published between January 2005 and August 2006. Phase four: MEDLINE was searched for primary studies published between September 2006 and August 2007. A search of one database only was carried out in the final phase in order to identify any studies published since the main searches were performed in August 2006. No language restriction was applied. Only full reports from 1990 were considered. The *International Journal of Obesity* and *Obesity* were handsearched online from January 2006 to September 2007 in order to identify studies that were not yet indexed on electronic databases.

Where results from studies could be quantitatively combined meta-analyses were undertaken. Data from RCTs and CBAs were analysed separately. Data synthesis (including handling of missing data) and quality assessment were based on those previously undertaken (7). For continuous data a weighted mean difference (WMD) was calculated (weighted by the inverse of the variance of the effect estimate) and Mantel–Haenszel methods were applied for dichotomous data, both using a fixed effects approach and RevMan 4.2.5 software (8). In the case of missing standard deviations (SDs) for changes in weight and risk factors, assumptions were made (irrespective of whether the changes were negative or positive). A linear regression was made of the SD of the mean change in weight on the absolute mean change for weight, for the studies that provided these data, and used to impute values for missing SDs:

- SD of weight change in kg = 5.915 + (0.283 × mean change in weight).

 

Similar linear regressions were attempted for risk factors. However, clear relationships were not found, so the means of reported SDs were used to impute values for missing SDs:

- SD for change in systolic blood pressure (SBP) = 12.7 mmHg.
- SD for change in diastolic blood pressure = 8.3 mmHg.
- SD for change in cholesterol = 1.08 mmol/L.
- SD for change in low-density lipoprotein (LDL) cholesterol = 0.74 mmol/L.
- SD for change in high-density lipoprotein (HDL) cholesterol = 0.29 mmol/L.
- SD for change in triglycerides = 0.96 mmol/L.

In the case of fasting plasma glucose and HbA1c, two levels of SDs were used to allow for the greater variability of such measures evident from the studies.

- If the initial fasting plasma glucose was <7 mmol/L, the SD for change in fasting plasma glucose was 1.35 mmol/L.
- If the initial fasting plasma glucose was ≥7 mmol/L, the SD for change in fasting plasma glucose was 3.77 mmol/L.
- If the initial HbA1c was <7%, the SD for change in HbA1c was 0.71%.
- If the initial HbA1c was ≥7%, the SD for change in HbA1c was 2.58%.

Results were described separately for individual studies where the change in outcome data between two time points could not be calculated or the number of participants in each group was not reported.

## Results

### Literature search

Thirty-nine RCTs (9–63) and one CBA (64) were included (Fig. S1, Table S1). Twenty-four studies were USA-based, four were based in Finland, three in the Netherlands, two in the UK (27,28), two in Canada, two in India and one each in Germany, Italy and Australia. Eight were community studies and 32 were in secondary care. Twenty studies were 24 months in duration, 11 studies were between 30 and 36 months in duration and nine studies ranged in duration from 38 to 97 months. Twenty studies recruited 200–2000 participants and five studies recruited over 2000 participants. In studies with fewer than 200 participants; sample size ranged from 16 to 180. The largest study was the Women's Health Initiative Dietary Modification Trial (WHIDMT) (42,45,46,61,62) with nearly 49 000 women.

Twenty-five studies recruited men and women, 14 studies recruited women and one study recruited men. At least 29 studies recruited participants with risk factors for disease, history of disease or disease, such as hypertension, type 2 diabetes and breast cancer. Mean baseline BMI was <30 kg $m^{-2}$ in 22 studies, unclear in two studies and ≥30 kg $m^{-2}$ in 16 studies. The majority of studies had a mean age between 40 and 60 years.

Twenty-four studies specifically intended participants to lose weight and 16 did not. Thirty-two studies included two comparison groups only (Table S2). Forty studies provided 39 different comparisons. There were no long-term studies identified that compared an exercise intervention with control.

Reports of the 39 RCTs (9–63) varied in quality with 12 clearly reporting allocation concealment, 10 applying an intention-to-treat analysis and two reporting effective blinding of outcome assessors (Table S3).

### Study results (Table S4)

#### *Studies with an intention to lose weight*

Dietary interventions vs. control

*600 kcal/day deficit diet deficit/low-fat diet vs. control*

Five studies assessed a 600 kcal/day deficit diet deficit/low-fat diet (21,22,24,30,33,34). Three studies recruited people with hypertension or 'high normal' blood pressure, one study recruited patients with oesophageal cancer and one recruited participants with IGT.

Weight. 600 kcal/day deficit diet deficit or low-fat diet was associated with non-significant weight changes at 24 and 30 months. However at 36 months, the Hypertension Prevention Trial (22) (HPT) was associated with a significant WMD weight change of –3.49 kg (95% confidence interval [CI] –4.63 to –2.35 kg).

Two studies were not included in the meta-analyses. Kristal *et al.* (24) reported a non-significant intervention effect on weight compared with control at 36 months (–1.4 kg). Ramachandran *et al.* (30) reported a significant increase in weight from baseline at 24 and 30 months in the control group (approximately 0.8 and 0.95 kg respectively) and at 24 months only in the diet group (approximately 0.4 kg).

Risk factors. In the HPT (22), blood pressure improved with diet at 36 months but did not reach statistical significance.

Clinical outcomes. Participants receiving diet in the Hypertension Optimal Treatment (21) (HOT) study required significantly fewer antihypertensive medications. Nine per cent of intervention and control groups required drug treatment for hypertension during the 3 years of the HPT (22). Weight loss increased the likelihood a patient

 

would be controlled on antihypertensive monotherapy in the Trial of Antihypertensive Interventions and Management (TAIM) study (33–35).

In Ramachandran *et al.* (30) the cumulative incidence of diabetes at 3 years was 55% in the control group and 39.3% in the diet group. Relative risk reduction was 28.5% compared with control.

*Low-calorie diet vs. control*

Weight. One study (38) was associated with a significant WMD weight change of –7.00 kg (95% CI –10.99 to –3.01 kg) at 24 months and –6.10 kg (95% CI –10.71 to –1.49 kg) at 36 months in 54 women treated for breast cancer. Wide CIs reflect the small sample size and there was nearly 40% dropout at 36 months.

*Weight Watchers vs. self-help*

Weight. One study (20) of Weight Watchers was associated with a significant WMD weight change of –2.70 kg (95% CI –3.95 to –1.45 kg) at 24 months (423 adults, majority women, BMI 34 kg $m^{-2}$).

Risk factors. Authors reported no significant difference between groups for risk factors or quality of life at 24 months.

*600 kcal/day deficit diet deficit/low-fat diet plus meal replacements vs. control*

Weight. One study (64) of a 600 kcal/day deficit diet deficit/low-fat diet using meal replacements (Slimfast shakes twice daily for 3 months then once daily for 57 months) compared with a no-contact matched control group was associated with a WMD weight change of –11.49 kg (95% CI –12.98 to –10.00 kg) at 2 years.

*Very-low-calorie diet using meal replacements (Cambridge diet) vs. low-fat control*

Weight. There was a non-significant weight change in favour of VLCD at 24 months among 16 obese Finnish adults with newly diagnosed type 2 diabetes (31). Risk factor data were not assessed as there were significant baseline differences between groups.

Behavioural interventions vs. control

Weight. Behaviour therapy delivered either by telephone or mail by trained nutritionists vs. control showed no significant effect on weight at 24 months in US adults from a managed care organization (54). Cost-effectiveness of telephone counselling was $132/kg lost, with mail and usual care control achieving similar cost-efficiency of $72/kg lost.

Diet and exercise vs. control

Three RCTs (18,19,26,28,59) assessed diet and exercise and all participants were at high risk of or had IGT. The types of diet and exercise interventions varied between studies (Table S1).

Weight. Diet and exercise were associated with significant WMD weight change at 24 months (–2.56 kg, 95% CI –3.34 to –1.77 kg).

Risk factors. There was an associated improvement in triglycerides in two studies (26,28) (WMD –0.54 mmol/L, 95% CI –0.85 to –0.24 mmol/L) and fasting plasma glucose in three studies (18,19,26,28,59) (WMD –0.30 mmol/L, 95% CI –0.42 to –0.18 mmol/L) but not cholesterol, blood pressure or HbA1c.

Clinical outcomes. At 4 years the cumulative incidence of diabetes in the Finnish Diabetes Prevention Study (FDPS) was 11% (95% CI 6–15%) in the intervention group and 23% (95% CI 17–29%) in the control group (risk of diabetes reduced by 58%). At 6 years there was a 43% reduction in relative risk (RR) (18,19). Normal glucose tolerance was present in 50% of intervention participants and 29% of control participants after 2 years in the study by Mensink *et al.* (26) ($P < 0.05$). In the FDPS, at mean follow-up of 3.9 years, 62.6% intervention participants and 71.2% control participants had metabolic syndrome (sex- and age-adjusted odds ratio [OR] 0.62 [95% CI 0.40–0.95]) (59).

Diet, exercise and behaviour therapy vs. control

Five RCTs (16,17,23,25,27,36,37) assessed diet, exercise and behaviour therapy. The types of diet and exercise interventions varied between studies (Table S1).

Weight. Diet and exercise and behaviour therapy were associated with significant WMD weight changes at 24 months (–2.47 kg, 95% CI –3.18 to –1.77 kg, two studies), 30 months (–2.04 kg, 95% CI –2.70 to –1.39 kg, two studies) and 54 months (–2.50 kg, 95% CI –3.59 to –1.41 kg, one study).

We were unable to meta-analyse the Diabetes Prevention Programme (DPP) (16,17); however, the authors reported that average weight loss at 2.8 years was 5.6 kg in the intensive low-fat diet, exercise and behavioural modification programme and 0.1 kg in the control group. Kuller *et al.* (25) did not present participant numbers for the 30- and 42-month follow-up; however, the authors reported significant improvement in weight.

Risk factors. The benefit of significant weight loss was not consistently reflected in improved risk factors. Although

 

Kuller *et al.* (25) demonstrated significant weight loss and improvements in LDL cholesterol, there was no significant improvement in HDL cholesterol, triglycerides, fasting plasma glucose or blood pressure at 54 months. The Trials of Hypertension Prevention phase II (36,37) study demonstrated significant weight loss and showed significant improvement in systolic but not diastolic blood pressure at 30 months.

Clinical outcomes. The DPP (16,17) significantly reduced the risk of developing diabetes and the metabolic syndrome for up to 3 years in over 2000 obese adults with IGT at baseline.

In the DPP (16,17) the crude incidence of diabetes was 11/100 in the control group and 4.8/100 in the lifestyle intervention. The incidence of diabetes was 58% lower (95% CI 48–66%) in the lifestyle intervention group than the control. The estimated cumulative incidence of diabetes at 3 years was 28.9% in the control and 14.4% in the lifestyle intervention group. Incidence of metabolic syndrome was reduced 41% in the lifestyle intervention compared with control ($P < 0.001$).

In the Trials of Hypertension Prevention phase II (36,37), the RR of developing hypertension for the weight loss group was 0.87 ($P = 0.06$) at 48 months.

### Adjuncts to diet

The addition of extra fruit and vegetables and exercise to a low-fat low-cholesterol diet was associated with a weight change of –6.10 kg compared with –2.1 kg in the low-fat low-cholesterol group at 36 months in mostly men with or at risk of coronary artery disease (32). Authors reported significant improvement in cholesterol, triglycerides, fasting blood glucose and blood pressure.

The addition of exercise and behaviour therapy to diet was associated with a non-significant difference in weight loss between groups at 24 months in one study of obese adults with type 2 diabetes (10). A significant improvement in total cholesterol was found at 24 months (–0.3 mmol/L [95% CI –0.6 to –0.1 mmol/L]) but not for blood pressure.

The addition of meal replacements (Slimfast) to a low-fat diet for the initial 3 months was associated with a non-significant weight change at 27 months but a significant weight change at 51 months (–5.40 kg, 95% CI –8.97 to –1.83 kg) (14,15,43). There was significant improvement in HDL cholesterol at 27 months (0.17 mmol/L, 95% CI 0.03 to 0.31 mmol/L) and SBP at 51 months (–12.0 mmHg, 95% CI –17.75 to –6.25 mmHg) but not other risk factors.

Women who received meal replacements (Slimfast) as part of low-fat diet, exercise and behaviour therapy provided in group sessions by a dietitian maintained the greatest weight loss at 2 years (WMD weight change –6.00 kg [95% CI –10.19 to –1.81 kg]) (9). However, dropout was 65% at 24 months. The addition of meal replacements was associated with significant improvement in HDL cholesterol (0.01 mmol/L, 95% CI 0.00–0.02 mmol/L) and glucose at 24 months (0.03 mmol/L, 95% CI 0.00–0.05 mmol/L) but not other risk factors.

The addition of pre-packaged food provision or financial incentives, or both combined and compared with a low-calorie diet, exercise and behaviour therapy intervention, did not significantly improve weight loss at 30 months in 200 overweight US adults in their late 30s (23).

### Head-to-head comparisons

One study of higher energy expenditure (2500 kcal/wk) through exercise and increased social support plus small monetary incentives compared with 1000 kcal/wk was associated with a non-significant weight change at 30 months (55). Both groups received low-fat diet and standard behaviour therapy.

There was no significant difference in weight between delivering behaviour therapy by telephone compared with mail in 1801 obese US adults from a managed care organization at 24 months (54).

There was no significant difference in weight at 24 months between women who were seen by a dietitian in a group and women seen by a nurse or physician in a clinic. Both groups received low-fat diet including meal replacements, exercise and behaviour therapy (9).

Glucose (0.03 mmol/L, 95% CI 0.01–0.05 mmol/L) and LDL cholesterol (0.02 mmol/L, 95% CI 0.01–0.03 mmol/L) were significantly improved in the nurse/physician group compared with the dietitian group at 24 months. There was significant difference in favour of lowered SBP for the dietitian group (–17.00 mmHg, 95% CI –27.91 to –6.09 mmHg). No other risk factor data were significantly different (9).

## Studies where the primary intention was not to lose weight

### Dietary interventions vs. control

Weight. A low-fat non-reducing diet was associated with a statistically significant weight change of –1.42 kg (95% CI –2.10 to –0.74 kg) at 24 months from two studies (13,39,40). Both studies were in women of normal weight who had either survived breast cancer or were at risk of breast cancer.

Two other studies reported weight change. There was a significant reduction in weight in the intervention group compared with the control at 24 months (approximately –1.6 kg vs. +1.5 kg respectively) in the feasibility trial for the Women's Intervention Nutrition Study (WINS) (41). In another study the intensive diet group increased mean weight by 2.09 kg and the routine diet group increased

 

weight by 1.57 kg at a median of 51 months of follow-up (57). There was a significant difference in the follow-up duration (median 58.6 months for intensive diet and 47.9 months for routine diet).

Clinical outcomes. There was no significant difference in the incidence of diabetes at 51 months in women of normal weight with a recent history of gestational diabetes (57), 6.1% for the intensive diet group and 7.3% for the routine diet group, an incidence rate of 0.83 (95% CI 0.47–1.48, $P = 0.50$).

A low-fat non-reducing diet significantly reduced the area of mammographic density (a risk factor for cancer) compared with control at 2 years (13).

### Behavioural interventions vs. control

Weight. Behaviour therapy vs. control showed no significant effect on weight at 24 months (one study of 115 physically active Canadian undergraduates, mean age 20 years, mean BMI 22.4 kg $m^{-2}$) (50).

Risk factors. There were no significant differences between groups in total cholesterol or HDL cholesterol; however, there was a significant difference in favour of behaviour therapy for triglycerides at 24 months (–0.20 mmol/L, 95% CI –0.40 to 0.00 mmol/L) (50).

### Diet and exercise vs. control

Weight. Diet and exercise education – with or without financial incentives – did not prevent weight gain in 809 overweight but otherwise healthy adults in one community-based study (Pound of Prevention) at 24 and 36 months (29). For diet and exercise, diet and exercise with incentives, and control, weight change was +1.3, +1.2 and +1.4 kg at 2 years and +1.6, +1.5 and +1.8 kg at 3 years respectively.

### Diet and behaviour vs. control

Four studies (42,45,46,52,58,60–63) ranged in size from 2079 participants to 48 835 women. The Polyp Prevention Trial (PPT) (52,60) recruited men and women with a recent large-bowel adenomatous polyp; two studies, Women's Healthy Eating and Living (WHEL) (58) and WINS (63), recruited women with previously treated or resected early-stage breast cancer, and the WHIDMT (42,45,46,61,62) recruited postmenopausal women.

Weight. Diet and behaviour therapy was associated with a significant weight change of –1.01 kg (95% CI –1.34 to –0.68 kg, two studies) at 24 months, –1.77 kg (95% CI –1.94 to –1.59 kg, three studies) at 36 months (Fig. S2), –0.52 kg (95% CI –0.85 to –0.19 kg, two studies) at 48 months and –0.70 kg (95% CI –0.90 to –0.50 kg, one study) at 90 months. The difference in weight was not significant at 72 months. There was significant heterogeneity between the studies.

WINS (63) reported a difference between intervention and control (in favour of intervention) of –1.8 kg (95% CI –3.1 to 0.2 kg) at 3 years and –2.7 kg (95% CI –4.5 to –0.9 kg) at 5 years.

Risk factors. Despite significant weight loss, the PPT (52,60) showed no significant difference between groups for cholesterol at 24, 36 and 48 months.

Clinical outcomes. Diet and behaviour therapy interventions did not significantly reduce incident cancers, including colorectal, breast, endometrial or ovarian cancer (61), risk of recurrent adenomatas (60) or mortality from colorectal or breast cancer (45,46) over 8 years. However, interim results suggest that intervention women in WINS (63) had a 24% lower risk of relapse events than women in control at 5 years (hazard ratio [HR] 0.76, 95% CI 0.60–0.98).

The WHIDMT showed no significant difference in overall incidence of ovarian cancer (HR 0.83, 95% CI 0.60–1.14) and cancer of the endometrium (HR 1.11, 95% CI 0.88–1.40) at 8.1 years. However, ovarian cancer risk was lower in the intervention group for the final 4 years (HR 0.60, 95% CI 0.38–0.96) (61). HR for colorectal cancer was 1.08 (95% CI 0.90–1.29) and mortality from colorectal cancer was 1.26 (95% CI 0.85–1.85) over 8.1 years (45,46). HR for breast cancer was 0.91 (95% CI 0.83–1.01) and mortality from breast cancer was 0.77 (95% CI 0.48–1.22) (45,46). HR for confirmed breast cancer event was 0.96 (95% CI 0.80–1.14; $P = 0.63$) in the WHEL (58) study over 7.3 years.

Risk of recurrent adenomatas was not significantly reduced in intervention participants of the PPT at 4 or 8 years (RR 0.98, 95% CI 0.81–1.39 at 8 years) (60).

The WHIDMT found no evidence for reducing diabetes risk after 8.1 years (HR 0.96, 95% CI 0.90–1.03) (62).

### Diet, exercise and behaviour therapy vs. control

Weight. Diet and exercise and behaviour therapy (clinic-based or home-based) was associated with non-significant weight changes at 24 and at 36 months compared with control in 284 healthy women in their mid-30s (53).

## Adjuncts to diet

### Diet plus exercise vs. diet

Two RCTs set in Finland were included (11,12,49). One study was community-based and recruited 90 men at risk of developing the metabolic syndrome (BMI 30–40 kg $m^{-2}$, waist circumference >100 cm) (11,12). The other (49)

 

recruited 82 women, mean age 40 years, mean BMI 34 kg $m^{-2}$. Both included studies had a VLCD of 8–12 weeks and had a mean weight loss of 13.1–14.3 kg prior to randomization.

Weight. The addition of exercise to a low-fat diet was associated with a non-significant weight change at 29–33 months, irrespective of type (walking or resistance training) or amount (3.6–8.4 MJ/wk) (Fig. S3). Men randomized to the walking group had 33% dropout compared with 13% dropout in the resistance training group (11,12).

Risk factors. The addition of exercise to a low-fat diet did not improve risk factors in women at 33 months (49).

Clinical outcomes. The OR for the occurrence of metabolic syndrome (from 2 months prior to randomization, both groups combined) was 0.29 (95% CI 0.16–0.50) (11,12).

### Other comparisons

A Mediterranean diet with behaviour therapy vs. a standard low-fat diet was associated with significant weight change at 24 months (–2.80 kg, 95% CI –3.06 to –2.54 kg) in 180 sedentary Italian adults with metabolic syndrome (48). There were significant improvements in total cholesterol (–0.23 mmol/L, 95% CI –0.26 to –0.20 mmol/L) and HDL cholesterol (0.07 mmol/L, 95% CI 0.06 to 0.08 mmol/L), triglycerides (–0.21 mmol/L, 95% CI –0.23 to –0.19 mmol/L), glucose (–0.33 mmol/L, 95% CI –0.37 to –0.29 mmol/L) and blood pressure (SBP –3.00 mmHg, 95% CI –3.46 to –2.54 mmHg; diastolic blood pressure –2.00 mmHg, 95% CI –2.29 to –1.71 mmHg) at 24 months.

A low-fat non-reducing vegan diet compared with a low-fat non-reducing diet was associated with a non-significant weight change at 24 months in 62 overweight postmenopausal women (56). Participants offered group support for 1 year after the initial intervention (regardless of group) lost more weight at 24 months compared with participants not offered group support. Vegan-supported participants lost significantly more weight than unsupported vegan participants at 24 months (–4.95 kg; 95% CI –7.50 to –2.40 kg) (Fig. S4).

There was no significant difference in weight between clinic-based diet, exercise and behaviour therapy and home-based diet, exercise and behaviour therapy at 24 and 36 months in 284 healthy normal-weight women in their mid-30s (53).

There was no significant difference in BMI between supervised group-based higher-intensity exercise set in the community vs. unsupervised individual higher-intensity home-based exercise (51). There was no significant difference in BMI between unsupervised individual higher-intensity home-based exercise and unsupervised individual lower-intensity home-based exercise (51). There were no significant differences between groups for risk factors.

There was no significant difference in weight between traditional structured exercise and behaviour therapy vs. lifestyle physical activity and behaviour therapy at 24 months in 237 sedentary, overweight adults (47). Only triglycerides were significantly improved in participants in the traditional structured exercise group compared with lifestyle physical activity at 24 months (–0.18 mmol/L, 95% CI –0.33 to –0.03 mmol/L).

There was no significant difference in weight or risk factors between exercise to expend 8.4 vs. 4.2 MJ/wk (both groups received diet) at 33 months in 82 obese premenopausal women (49).

There was no significant difference in weight between walking (5.2 MJ/wk) and resistance training (3.6 MJ/wk) at 31 months in 90 obese men (11,12).

Low-fat non-reducing diet and exercise with incentives compared with low-fat non-reducing diet and exercise without incentives did not prevent weight gain in 809 overweight but otherwise healthy adults in one community-based study at 24 and 36 months (29). Diet with exercise and incentives vs. diet with exercise; weight change was +1.2 vs. +1.3 kg at 2 years and +1.5 vs. +1.6 kg at 3 years.

## Deaths and clinical outcomes

Meta-analyses showed no significant difference between lifestyle interventions and control groups for deaths (Fig. S5), stroke, heart disease or cancer outcomes. Diet and behaviour therapy suggested reduced risk of breast cancer recurrence at 5 years (63) and ovarian cancer in the final 4 years of an 8-year trial (61).

Interim results suggest that intervention women in WINS (63) had a 24% lower risk of breast cancer recurrence than women in control at 5 years (HR 0.76, 95% CI 0.60–0.98). Ovarian cancer risk was lower in the intervention group for the final 4 years (HR 0.60, 95% CI 0.38–0.96) of the WHIDMT (61).

There is evidence that lifestyle intervention can prevent diabetes and the metabolic syndrome. Two studies were terminated early (16,17,30) as a result of unequivocal evidence of effectiveness of the lifestyle intervention in significantly reducing the risk of developing type 2 diabetes.

The DPP (16,17) demonstrated that an intensive low-fat diet, exercise and psychological support intervention compared with control can prevent the metabolic syndrome at 3 years (OR 0.54, 95% CI 0.42–0.69). Combined data from the DPP (16,17) and a study of Mediterranean diet and behaviour therapy vs. standard low-fat diet (48) showed that these interventions can resolve cases of the metabolic syndrome for up to 3 years (RR 2.52, 95% CI

 

2.08–3.05) (in this case an RR of greater than 1 favours treatment as higher resolution indicates a better outcome). In the FDPS (59), at mean follow-up 3.9 years, 62.6% intervention participants and 71.2% control participants had metabolic syndrome (sex- and age-adjusted OR 0.62 [95% CI 0.40–0.95]).

Three studies (18,19,27,30,59) (diet vs. control; diet and exercise vs. control; diet, exercise and behaviour therapy vs. control) showed a significant effect on the prevention of type 2 diabetes up to 6 years (RR 0.68, 95% CI 0.57–0.82). This result is consistent with the results from the DPP (16,17) in which the incidence of diabetes was 58% lower (95% CI 48–66%) in the intensive lifestyle intervention group than the control. However, the WHIDMT (62) showed no evidence of reducing diabetes risk after 8.1 years.

## Discussion

This systematic review captured a relatively large number of studies (40), capturing interventions aimed at preventing weight gain in adults who were of normal weight, overweight and obese. In doing so, it extends the evidence base beyond a recent review (65).

Eleven of 39 comparisons produced significant improvement in weight, of which eight compared an intervention to a non-treatment control. Eight intended to produce weight loss and produced greater weight loss than the three studies not intending weight loss (WMD weight change 2.0–11.5 vs. 0.5–2.8 kg respectively). 600 kcal/day deficit diet deficit/low-fat diets with and without meal replacements, low-calorie diets, Weight Watchers, low-fat non-reducing diets, diets with behaviour therapy, exercise or exercise and behaviour therapy produced significant improvement in weight compared with control. Weight loss ranged from –0.5 to –11.5 kg. Adding meal replacements produced significant improvement in weight, particularly in the long-term. Direct comparisons of interventions failed to show significant effect on weight with the exception of Mediterranean diet and behaviour therapy compared with a low-fat diet.

Interventions combining diet with additional elements compared with control were not always associated with greater weight loss. Both diet and exercise and diet, exercise and behaviour therapy produced similar weight changes, less than some of the diets alone and similar to that achieved by Weight Watchers (20). There was insufficient evidence to assess the benefit of adding exercise or behaviour therapy. There were no studies that assessed the effectiveness of adding behaviour therapy or exercise and behaviour therapy to a non-reducing diet. There did not appear to be any obvious pattern between intensity of contact or diet prescription and weight change.

The four meal replacement studies (9,14,15,31,43,64) began with an intensive phase consisting of meal replacements two to three times daily for 3 months, then three studies continued to use meal replacements less often (in one study both groups received meal replacements for the maintenance period). Significant benefit to weight was demonstrated in the two studies that assessed the addition of meal replacements in the maintenance phase, although one of these was not a randomized study (64).

Risk factor data were limited; weight loss did not consistently improve risk factors; some risk factors improved independent of weight change. Another review including lifestyle interventions of at least 2 years in duration found that weight loss of at least 5% baseline weight was not consistently associated with improvement in cardiovascular risk factors and benefits were specific to the intervention and occurred mainly in people with cardiovascular risk factors (66).

Few studies were powered to detect differences in morbidity and mortality or followed up participants for sufficient time. There was no significant difference between lifestyle interventions and control groups for deaths, stroke, heart disease or cancer. Diet and behaviour therapy suggests reduced risk of breast cancer recurrence at 5 years (63) and ovarian cancer in the final 4 years of an 8-year trial (61). 600 kcal/day deficit diet deficit/low-fat diets can reduce type 2 diabetes, improve blood pressure and reduce antihypertensive medication for up to 3 years. Diet and exercise reduce the risk of type 2 diabetes for up to 6 years and the metabolic syndrome at 4 years, compared with control. Diet with exercise and behaviour therapy can reduce the risk of type 2 diabetes, hypertension and the metabolic syndrome. The addition of exercise to diet can reduce the risk of metabolic syndrome in men. However, a non-reducing diet and behaviour therapy did not reduce diabetes risk in nearly 49 000 women after 8.1 years (62).

Research is required into whether effectiveness of interventions varies with baseline risk, age, gender, ethnic group and setting. WHIDMT (62) suggests that relatively small amounts of weight loss without increase in physical activity may account for why the intervention did not reduce the risk of diabetes compared with the FDPS (18,19,59) and DPP (16,17,44). Participants in the FDPS and DPP were at higher risk of developing diabetes and had higher baseline BMI compared with the WHIDMT. In the DPP (44), lifestyle intervention was most effective in preventing diabetes in older participants (60–85 years) perhaps as a result of greater weight loss and physical activity. Interim analysis of WINS (63) diet and behaviour intervention suggests significantly reduced risk of breast cancer recurrence in postmenopausal women, whereas the WHIDMT (42,45,46,61,62) and WHEL (58) studies did not significantly reduce breast cancer morbidity. Women in the dietary intervention arm of WINS lost more weight than the other studies, which may account for the lowered risk.

There was scant reporting of economic or quality of life data. The FDPS was used to assess whether a lifestyle

 

intervention to prevent diabetes in adults with IGT is cost-effective in a Swedish setting (67). The model predicted that the intervention would be cost-saving, with an increase in estimated survival of 0.18 years. The predicted cost-effectiveness ratio was €2363 per quality-adjusted life year gained.

It was difficult to determine whether some studies were supposed to affect weight or not, or whether exercise or behaviour therapy was provided, and to classify types of diet. Classification of interventions was difficult because the information reported within the papers was insufficient; classification was often arrived at by a consensus process between reviewers. Where the calorie content of a diet was not clearly stated it was categorized as a '600 kcal/day deficit diet deficit or low-fat diet' (where there was a definite intention to provide weight loss) or 'low-fat non-reducing diet' (where there was no definite intention to provide weight loss). For exercise or behaviour therapy interventions to be categorized as such, study investigators had to give a detailed description of the components of the intervention.

Studies were heterogeneous and the varied comparisons were underpinned by few studies, making it difficult to generalize about effective interventions. There were inadequate data reported to include some studies in meta-analyses; in addition, it was necessary to calculate weight and risk factor change from absolute values or from graphs that meant that SDs needed imputing in 25% of studies. A minority of studies reported adequate allocation concealment, intention-to-treat analyses or blinding of outcome assessors. It was not possible to assess the differential effects of interventions according to demographic, socio-economic or cultural characteristics (68).

There is limited evidence for lifestyle interventions to prevent weight gain in healthy normal-weight adults within the community. To widen the evidence base requires review of uncontrolled interventions and synthesis of evidence from complex public health interventions with new methods to assess evidence.

These gaps in the evidence base and inadequacies relating to study design and reporting necessitate recommendations for future interventions to be longer-term and sufficiently powered to detect clinical outcomes. Adequate reporting of outcome data would enable all studies to be included in meta-analyses (where relevant to do so). Detailed reporting of interventions, participant characteristics, economic and quality-of-life data would improve the quality of future systematic reviews of lifestyle intervention.

## Conclusion

Diet, alone and with the addition of exercise and/or behaviour therapy, demonstrated significant weight loss and improvement in metabolic syndrome and diabetes compared with no treatment control for at least 2 years.

## Conflict of Interest Statement

No conflict of interest was declared.

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## Supporting information

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Flow diagram for locating primary studies of controlled trials for systematic review.
**Figure S2.** Diet and behaviour therapy vs. control at 36 months. No intention to lose weight. PPT, Polyp Prevention Trial; WHEL, Women's Healthy Eating and Living; WHIDMT, Women's Health Initiative Dietary Modification Trial.
**Figure S3.** Diet and exercise vs. diet at 29/33 months. No intention to lose weight.
**Figure S4.** Low-fat vegan diet vs. low-fat NCEP diet at 24 months. No intention to lose weight.
**Figure S5.** Overall deaths.
**Table S1.** Table of included studies.
**Table S2.** Overview of included studies.
**Table S3.** Table of quality assessment of RCTs.
**Table S4.** Table of weight results from meta-analyses.
**Appendix S1.** Search strategies.

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